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Study Title

Executive Summary Review of Sodium Chlorite/Chlorine Dioxide
For Use on Field Grown Wheat, Barley, and Oats

Data Requirement

Non-Guideline Requirements

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Statement of Data Confidentiality Claim

No information is claimed confidential on the basis of its falling within the scope of FIFRA § 10(d)(1)(A), (B), or (C).

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Date: August 3, 2005

Good Laboratory Practices Statement

This review, titled "Executive Summary Review of Sodium Chlorite/Chlorine Dioxide for Use on Field Grown Wheat, Barley, and Oats" is a discussion and presentation of compiled information from published literature. No data are being submitted that are subject to Good Laboratory Standards (40 CFR Part 160).

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August 3, 2005

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INTRODUCTION

In a pre-registration meeting on November 16, 2004, Bi-Oxide Crop Science LLC (Bi-Oxide), requested data waivers for the agronomic food/feed use of sodium chlorite when used on field grown wheat, barley and oats. The U.S. Environmental Protection Agency (EPA) (Agency) Office of Pesticide Programs Registration Division (RD) found this request to be acceptable since the sodium chlorite/chlorine dioxide chemistry is well known. In the meeting it was noted that the Anti-Microbial Division (AD) had approved the use of chlorine dioxide / sodium chlorite on stored potatoes. It was understood that acidified sodium chlorite will convert to chlorine dioxide, which in turn will oxidize both organic and inorganic reducing agents and that it is this oxidative mechanism that provides fungicidal activity. It was also understood that Bi-Oxide would not be required to generate new data, but instead could submit data waiver requests in the form of literature reviews and these could be submitted following the reporting format as outlined in PR Notice 86-5. This executive summary serves as a review of how Bi-Oxide has addressed all of the data requirements as would be required to register the sodium chlorite product on wheat, barely, and oats and to obtain exemptions from the requirement of tolerances for these small cereal crops. As detailed in the pre-registration meeting, Bi-Oxide is seeking a Formulator's Exemption Registration and will rely on Vulcan Chemical (Vulcan) in support of the new registration. Vulcan is currently a registrant of technical sodium chlorite. It should be noted that the current Vulcan data only supports anti-microbial uses and does not support all of the data requirements as would be required for field grown crops. It is these missing data requirements (Vulcan data) that Bi-Oxide is requesting data waivers for.

BACKGROUND

The Bi-Oxide product is an ionic solution that contains 25% sodium chlorite (active ingredient). Prior to use, the product will be diluted in water and an approved inert acid will be added to the solution. The theoretical maximum conversion of sodium chlorite to chlorine dioxide is 80% (Vulcan, TDS 600-103).

In the presence of a mono-valent acid, such as hydrochloric, the following reaction is expected to occur:

$$5NaClO_2 + 4HCl \rightarrow 4ClO_{2(g)} + 5NaCl + 2H_2O.$$

In the presence of a divalent acid, such as sulfuric acid, the following reaction is expected to occur:

$$4NaClO_2 + H_2SO_4 \rightarrow 2ClO_{2(g)} + NaCl + NaClO_3 + 2NaSO_4 + H_2O.$$

From 50% to 70% of the reacted ClO_2 (chlorine dioxide) will be converted to ClO_2^- (chlorite) with the balance forming Cl^- (chloride) and ClO_3^- (chlorate).

In pure water, sodium chlorite and chlorine dioxide will exist in state of equilibrium. Chlorine dioxide (ClO_2) will oxidize phenolics, secondary and tertiary amines, and organic sulfides, as well as inorganic iron and manganese and will be subsequently reduced to chloride. The chlorite ion will also function as an oxidizing agent; however it will be reduced at a slower rate than chlorine dioxide. The measurable terminal residue for sodium chlorite is also chloride.

Chlorine dioxide is currently used in water treatment management practices to disinfect drinking water of harmful bacterial and other microorganisms. For drinking water, EPA set a maximum concentration of 0.8 and 1.0 mg/L for chlorine dioxide and chlorite ion, respectively (Public Health Statement).

PROPOSED FIELD USE PATTERN

The proposed use pattern will involve a field application(s) of acidified sodium chlorite to field grown small grain cereals (including wheat, barley, and oats). Prior to a field application of the Bi-Oxide sodium chlorite product (25% active ingredient), an approved acid will be added (for activation purposes) along with water. The proposed seasonal use pattern is one (1) application at 0.16 lb ai / acre or two (2) applications at 0.1 lb ai/acre each, the second application following the first by 1 to 3 weeks, depending upon disease pressure. The single or first application would be made to field grown wheat, barley, and oats at the flowering stage. The application(s) will be made by either aircraft and/or ground operated equipment. Because the application(s) will be made at heading and due to typical heavy plant populations, the majority of the product is expected to be applied by aircraft. Aerial applications will use a minimum of 5 gallons of water per acre and ground applications will use between 10 to 20 gallons. Because of the potential corrosive nature of the active ingredient and the acid, the label will prohibit applications through irrigation systems (chemigation).

CURRENT DATA TO SUPPORT AGRICULTURAL USES

Bi-Oxide will re-package Vulcan Technical Sodium Chlorite Solution 31.25 (EPA Reg. No. 5382-43) (active ingredient sodium chlorite 25%) and will cite Vulcan data in support of a Formulator's Exemption Registration. Vulcan data covers the following requirements: (i) Product Chemistry §158 parts 155, 160, 162, 165, 167, 170, 175, 180, and 190; (ii) Toxicology §158.340; and (iii) Wildlife and Aquatic Organisms §158.490.

CURRENT EXEMPTIONS FROM THE REQUIREMENT OF A TOLERANCE

Sodium chlorite is currently exempt from the requirement of a tolerance when used as a seed-soak treatment in the growing of the raw agricultural commodities crop group *Brassica* (cole) leafy vegetables and radishes (§180.1070) and when used as a direct treatment at up to 400 ppm on potatoes going into storage (Brennis, Antimicrobial Division, August 5, 2003). Regarding potatoes, EPA stated, "It was determined that it is unlikely that there would be a residue of chlorine dioxide on the potatoes, so no food tolerance is required". The direct use on stored potatoes would represent a "worst case" use of a pesticide as compared to field use on cereals at flowering since this is a post-harvest use and no holding time restrictions were placed on potatoes following a treatment with sodium chlorite.

DATA WAIVER REQUESTS

Vulcan (EPA Reg. No. 5382-43) does not support the use of sodium chlorite for agronomic crop uses. Data gaps include the requirements for (i) Residue Chemistry §158.240; (ii) Environmental Fate §158.290; (iii) Reentry Protection §158.390; (iv) Spray Drift §158.440; (v) Plant Protection §158.540; and (vi) Nontarget Insect §158.590. In order to satisfy data requirements, Bi-Oxide has submitted data waiver request reports following PR Notice 86-5. The following are brief summaries of the data waiver request reports.

Magnitude of the Residue in Plants and Livestock (CRGC-2005-2)

The terminal residue in plants and animals is chloride. Under acidic conditions, sodium chlorite will covert to chlorine dioxide, which in turn will oxidize phenolics, secondary and tertiary amines, and organic sulfur groups and be subsequently reduced to chloride. Chlorite has been used as a laboratory agent to remove lignin from plant samples. When potatoes and strawberries were treated with activated chlorite, there were no measurable chlorine dioxide residues and chlorite residues were <0.07 ppm (detection limit). Chlorite residues are not expected to be present in wheat, barley, and oats a 3 weeks after treatment. And residues are not expected to occur in livestock that is feed treated grain and straw (cattle). With an exemption from the requirement of a tolerance, there would be no need for an analytical method or analytical reference standards.

Nature of the Residue (CRGC-2005-3)

Chlorite and chlorine dioxide are oxidizing agents that will react with organic reducing agents, such as phenolics, secondary and tertiary amines and organic sulfides to produce chloride, the terminal residue. A post-harvest potato study that used acid activated chlorite at 400 ppm in a direct mist form found no chlorine dioxide residue and found chlorite residues at <0.07 ppm on whole potatoes. When strawberries were treated and stored for one week at 4°C, there were no detectable residues of chlorine dioxide and residues of chlorite were 0.07 ± 0.12 ppm (detection limit). Chlorite is the expected residue for wheat, barley, and oats following a 3 week application time period. Chlorite residues are not expected to occur in livestock that would be feed either grain or straw.

Soil Dissipation (CRGC-2005-4)

Sodium chlorite and chlorine dioxide are oxidizing agents that will be reduced to chloride under soil conditions. Chloride dioxide has been used as a laboratory bleaching agent to oxidize soil organic matter samples. When soils with organic matter contents of 9.34 and 0.9% were treated with acidified sodium chlorite, chlorite residues were not detected at 4 hours and 8 days after treatment, respectively. Some soil bacteria have been identified to contain chlorite dismutase, which will reduce chlorite directly to chloride. Any chlorite capable of leaching to groundwater would be subject to oxidative reactions with sulfides, iron, and manganese as well as organic matter.

Photodegradation in Water (CRGC-2005-5)

Chlorine dioxide has a broad UV adsorption band with a maximum near 360 nm. Photodecomposition of chlorine dioxide typically increases as the wavelength decreases with Φ values of 0.65, 1.4, 1.4, 0.46, and 0.1 at 253.7 (average of three values), 296.7, 300, 366, and 400 nm, respectively. A proposed photolysis mechanism involves nine reactions of which two are primary photo-processes, four are bimolecular steps of chlorine dioxide with the primary photo-fragments or the radical chlorate ion producing chorine oxide intermediates, and three are hydrolysis reactions leading to stable products in solution. Water pH has little effect on chlorine dioxide or sodium chlorite photodegradation at 320 nm. The half life of chlorite is less than 30 minutes under natural sunlight. The half-lives of chlorine dioxide and sodium chlorite are approximately 4,500 J m^{-2} and 9,000 J m^{-2}, respectively at 253.7 nm. Under field conditions, when chlorine dioxide and sodium chlorite are exposed to sunlight, both would undergo rapid photodegradation and convert to chloride and hypochlorous acid.

Hydrolysis (CRGC-2005-6)

Hydrolysis is defined as a chemical reaction of an organic chemical with water in such a manner that one or more bonds (of the chemical) are broken and the reaction products incorporate the elements of water (H_2O). Sodium chlorite ($NaClO_2$) and chlorine dioxide (ClO_2) do not meet the basic definition since both are inorganic molecules and as such neither would be subject to hydrolysis.

Metabolism in Aerobic Soil (CRGC-2005-7)

Chloride is the terminal soil residue and results from one of two pathways. The major pathway involves chemical oxidation in which both organic and inorganic materials are oxidized and chlorite and chlorine dioxide are reduced to chloride. Chlorite is converted to chlorine dioxide under acidic conditions and chlorine dioxide will oxidize phenolics, secondary and tertiary amines, and organic sulfides. Chlorine dioxide will also oxidize inorganic iron and manganese. Chlorine dioxide is so reactive in a soil matrix that it has been used as a laboratory bleaching agent used to oxidize soil organic matter ring structures. The second and minor pathway involves an enzymatic reaction. Chlorite dismutase will convert chlorite directly to chloride and O_2. The same soil bacteria that contain this enzyme will also degrade perchlorate.

Sediment and Soil Adsorption/Desorption (CRGC-2005-8)

OPPTS 835.1220 (Sediment and Soil Adsorption/Desorption) states that it is "Not applicable to compounds which are unstable in the time scale of the test". Sodium chlorite and chlorine dioxide are both oxidizing agents and both are subject to reduction to chloride under conditions typical in soil and sediments. Chlorine dioxide is so reactive that it has been used as a laboratory reagent for bleaching soil samples. Because of its negative charge, chlorite would behave as a salt in a soil solution and adsorption to organic and clay surfaces would be limited.

Re-Entry Exposure Protection (CRGC-2005-9)

Mixers/loaders and applicators would be required to follow all label requirements regarding PPE and engineering controls. Due to the timing of the application(s) and crop density, fields would be kept free of human and machinery traffic since such activity would adversely impact yields. At a minimum post-harvest interval (PHI) of three week, treated fields would be harvested following standard agronomic practices. There would be little or no expected exposure due to physical exertion.

Foliar dislodgeable residues and bare treated soil should not present a risk. Any chlorite and/or chlorine dioxide residues on vegetation and soil would be rapidly converted to chloride and should therefore pose no risk to field workers.

A conservative maximum airborne concentration of sodium chlorite/chlorine dioxide in an area up to 10 ft above the canopy one hour after application is 1 ppb, assuming that 80% had either dissipated or had settled onto the canopy. The OSHA PEL (permissible exposure limit) 10 hour TWA (time weighted average) is 0.1 ppm (combined for sodium chlorite and chlorine dioxide) (29CFR1910.1000). If necessary, entry into a treated area one hour after treatment would be safe since the exposure would be 100 times less than the OSHA PEL. The draft label proposes a 24 hour re-entry after treatment. This time period would adequately remediate any potential issues involving airborne materials as could impact any potential inhalation risk.

A Pesticide Handlers Exposure Database (PHED) assessment found that the Margins of Exposure (MOE) were greater than 100 for combined inhalation and dermal exposure for mixers/loaders and applicators.

An EPA pharmacokinetics review of chlorine dioxide and chlorite found that the major urinary "metabolite" is chloride. The review also reported a plasma half-life of 8 hours following oral administration. Given that chloride is the major metabolite, there would be no useful purpose served by field monitoring.

Spray Drift (CRGC-2005-10)

A screening level risk assessment was conducted to determine if the activated sodium chlorite product would pose any risk to a wide variety of terrestrial, avian, and aquatic organisms. A conservative 5% default (based on GENEEC, version 1.3 and Birchfield [2004]) was used to determine the spray drift potential. Risk quotients (RQs) were compared to levels of concern (LOCs). No acute or chronic risk is expected for terrestrial organisms including mammals, earthworms (using a surrogate) and insects (including honey bees). No acute or chronic risk is expected for avian species including Bobwhite quail and Mallard duck. Based on the results of treatments to 15 different herbaceous and woody plant species, no acute risk is expected to vegetation that would be exposed to a one time drift application with a 5% default spray drift. With the exception of daphnid (*Daphnia magna* and *Ceriodaphnia dubia*), the proposed sodium chlorite application is practically nontoxic to a broad range of nontarget aquatic organisms and because exposure is likely to be minimal with a 5% spray drift, acute risk is not expected. The risk quotients for fish and amphibians were <0.01. For water fleas, a food source for a number of fish, *Daphnia magna* and *Ceriodaphnia dubia* had LOCs of 0.02 and 0.09, while five other water fleas had LOCs of ≤ 0.01. With the exception of daphnid, there is no potential risk from spray drift to either terrestrial animals and plants or aquatic animals.

Non-Target Terrestrial Plants (CRGC-2005-11)

Sodium chlorite and chlorine dioxide are not expected to have an impact on seedling emergence. Since the sodium chlorite solution would be applied in a foliar manner to the proposed crops (wheat, barley, and oats), a seedling emergence assessment would involve applying the material to the soil surface using after planting seeds. When applied to soil, sodium chlorite and chlorine dioxide would convert to the terminal residue, chloride. Chlorine dioxide would not be expected to diffuse into the soil and if some did, it would rapidly oxidize organic and inorganic materials and convert to chloride. The chlorite would move through the soil as a negative charged anion; however in the presence of weak acids, as are typically exuded by soil microorganisms and in the presence of chlorite dismutase, chlorite would be converted to chloride. Due to the reductive capacity found in typical agronomic soils, the conversion of chlorine dioxide and chlorite to chloride would essentially insure that there would be little if any measurable effect on germination and seedling emergence.

Given the proposed use rates, sodium chlorite and chlorine dioxide are not expected to have an impact on vegetative vigor. Because of the differences in physical properties, sodium chlorite and chlorine dioxide would react differently in or on treated plant surfaces. As a gas, chlorine dioxide could potentially penetrate foliate. Because chlorine dioxide is so reactive in soil matrices, it is not expected that there would be any transfer of chlorine dioxide from the soil to growing plants. Since chlorite is an anion, volatilization is not expected and in a crystalline form, the chlorite would remain where it was deposited on plant tissue. Organic acids that are exuded from plant cells as well as the pH gradient that typically exists along cell walls would be expected to convert chlorite to chloride.

When chlorine dioxide was applied three times at 50 ppm each on three day intervals to 16 different ornamental plant types, the injury to the plants was less than 4%. These results demonstrated that foliage has a reduction capacity to handle such exposures. According to EPA published estimates, the estimated ppm level resulting from an application rate of 0.1 lb active ingredient per acre to a mixed grass and broadleaf mixture would be approximately 19 ppm. Given that multiple applications of 50 ppm had no significant effect on 16 different plant types, it could be assumed that there would be little or no effect on seedling vegetative vigor following the proposed label instructions.

Non-Target Pollinating Insects and Honey Bees (CRGC-2005-12)

The use of sodium chlorite and chlorine dioxide following the proposed label application rate(s) is not expected to present a risk to pollinating insects, including honey bees. If the full strength 25% active ingredient sodium chlorite solution were to be applied directly to honey bees and other pollinating insects, there could potentially be some mortality. However, the proposed use rate would be approximately 1 ppm per acre when applied to small cereals at the heading stage. This value was taken from EPA estimates when using the 0.1 lb active ingredient per acre use rate on long grass. This 1 ppm level would be the expected concentration that pollinating insects would encounter while in flight over a sprayed area or while alighted on an impacted plant during or immediately following an application. Chlorine dioxide at 10 and 100 ppm concentrations in sucrose significantly increased the life span of tested honey bees. The beneficial effect was most likely due to a reduction in viral, bacterial, and/or fungal pathogens that are normally present in or on the bees. When activated chlorite was applied directly to honeybee hives or was taken into the hive in a gel form by the bees, there was no toxic effect.

SUMMARY

Because of the reactive properties of these inorganic oxidizers, the use of sodium chlorite and chlorine dioxide is not expected to result in any residues of concern and is not expected to present a risk to non-target terrestrial and aquatic plants and animals and should present no risk to humans.